

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors:	Ghai et al.	Confirmation No.:	2837
Application No.:	10/088,664	Art Unit:	1651
Filed:	August 15, 2002	Examiner:	Kailash C. Srivastava
For:	EXTRACTS OF ORANGE PEEL FOR PREVENTION AND TREATMENT OF CANCER	Attorney Docket No.:	11592-006-999 (formerly RU- 0103-US)

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. §1.56 AND §1.97**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure imposed by 37 C.F.R. § 1.56 and § 1.97 to inform the Patent Office of all references coming to the attention of each individual associated with the filing or prosecution of the subject application, which are or may be material to the patentability of any claim of the application, Attorneys for Applicants hereby invite the Examiner's attention to the references **A01-A07**, **B01-B29** and **C01-C53** listed on the attached revised form PTO 1449 entitled "List of References Cited by Applicant." Copies of references **B01-B29** and **C01-C53** are submitted herewith.

Identification of the listed references is not meant to be construed as an admission of Applicants or Attorneys for Applicants that such references are available as "prior art" against the subject application. Consequently, Applicants respectfully decline to use form PTO-1449, since this form identifies all of the references cited therein as "Prior Art." As an alternative, Applicants submit herewith a "revised form PTO 1449" entitled "List of References Cited" instead of "List of Prior Art Cited".

Applicants respectfully request that the Examiner review the foregoing references and that the references be made of record in the file history of the application.

Since this Supplemental Information Disclosure Statement is being filed in the United States Patent and Trademark Office concurrently with a Request for Continued Examination under 37 C.F.R. § 1.114, pursuant to 37 C.F.R. § 1.97(b)(4), Applicants believe that no fee is

due. However, should the Patent and Trademark Office determine otherwise, please charge any required fee to Jones Day Deposit Account No. 50-3013. A duplicate of this sheet is enclosed for accounting purposes.

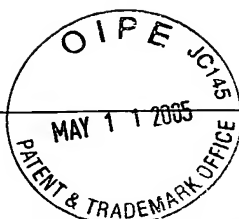
Date May 11, 2005

Respectfully submitted,

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**LIST OF REFERENCES CITED BY APPLICANT**

(Use several sheets if necessary)

ATTY. DOCKET NO.

11592-006-999

(formerly RU-0103-US)

APPLICATION NO.

10/088,664

APPLICANT

Ghai et al.

FILING DATE

August 15, 2002

GROUP

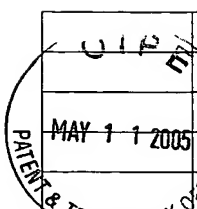
1651

**U.S. PATENT DOCUMENTS**

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A01	3,867,541	02/18/1975	Robbins			
	A02	3,903,266	09/02/1975	Robbins			
	A03	5,041,425	08/20/1991	Hasegawa et al.			
	A04	6,184,246	02/06/2001	Manthey et al.			
	A05	6,221,357	04/24/2001	Bok et al.			
	A06	6,239,114	05/29/2001	Guthrie et al.			
	A07	6,251,400	06/26/2001	Guthrie et al.			

**FOREIGN PATENT DOCUMENTS**

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	B01	CN 1049340	02/20/1991	China (with English abstract)				
	B02	CN 1069200	02/24/1993	China (with English abstract)				
	B03	CN 1071576	09/26/2001	China (with English abstract)				
	B04	CN 1094957	11/16/1994	China (with English abstract)				
	B05	CN 1100322	03/22/1995	China (with English abstract)				
	B06	CN 1105853	08/02/1995	China (with English abstract)				
	B07	CN 1108554	09/20/1995	China (with English abstract)				
	B08	CN 1139007	01/01/1997	China (with English abstract)				
	B09	CN 1145804	03/26/1997	China (with English abstract)				
	B10	CN 1170592	01/21/1998	China (with English abstract)				
	B11	CN 1191746	03/05/1998	China (with English abstract)				
	B12	CN 1279905	01/17/2001	China (with English abstract)				
	B13	CN 1301507	07/04/2001	China (with English abstract)				
	B14	DE 39 22 666	07/10/1989	Germany (abstract see A03)				
	B15	JP 2000-80035	03/21/2000	Japan (with English abstract)				
	B16	JP 2000-83654	09/14/1998	Japan (with English abstract)				
	B17	JP 2004-137218	05/13/2004	Japan (with English abstract)				
	B18	JP 3010210	12/10/1999	Japan (with English abstract)				
	B19	JP 60-199817	10/09/1985	Japan (with English abstract)				
	B20	JP 9-295932	11/18/1997	Japan (with English abstract)				
	B21	WO 1999/15167	04/01/1999	PCT (U.S.)				
	B22	WO 1999/52380	10/21/1999	PCT (Korea)				
	B23	WO 1999/62358	12/09/1999	PCT (Korea)				
	B24	WO 2000/07607	02/17/2000	PCT (U.S.)				

	B25	WO 2000/32062	06/08/2000	PCT (Israel)					
	B26	WO 2000/64282	11/02/2000	PCT (Italy)					
	B27	WO 2000/76492	12/21/2000	PCT (U.S.)					
	B28	WO 2001/51043	07/19/2001	PCT (U.S.)					
	B29	WO 2001/70029	09/27/2001	PCT (U.S.)					

**OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)**

C01	"Colon cancer prevention and citrus flavonoid," <i>Nutrition Research Newsletter</i> 17(7-8) (1998)
C02	"Fruit with a pun," <i>Natural Health</i> pp. 116-119, 187 (Jul.-Aug. 1998)
C03	"Fruitful findings on cancer," <i>Tufts University Diet &amp; Nutrition Letter</i> p. 6 (Aug 1996)
C04	Attaway, "Citrus juice flavonoids with anti-cancer properties," <i>Abstracts of Papers of the American Chemical Society</i> , 204:P184-AGFD (1992) [abstract]
C05	Boterberg et al., "Inhibition of the tamoxifen by the citrus flavonoid tangeretin: an NK cell mediated effect?" <i>Acta Clinica Belgica</i> 54(2):109 (1999) [abstract]
C06	Bracke et al., "Citrus flavonoid effect on tumor invasion and metastasis the citrus flavonoid tangeretin may inhibit the processes that shorten the life expectancy of tumor-bearing patients," <i>Food Technology, Institute of Food Technologists</i> , Chicago, US, 48(11):121-124 (1994)
C07	Bracke et al., "Influence of tangeretin on tamoxifen's therapeutic benefit in mammary cancer," <i>J. National Cancer Institute</i> 91(4):354-359 (1999)
C08	Bracke et al., "The citrus flavonoid tangeretin enhances cell-cell adhesion and inhibits invasion of human MCF-7/6 breast carcinoma cells," <i>Abstracts of Papers American Chemical Society</i> 208(1-2): pAGFD 81 [abstract] (1994)
C09	Bracke et al., "The flavonoid tangeretin inhibits invasion of MO <sub>4</sub> mouse cells into embryonic chick heart <i>in vitro</i> ," <i>Clin. Expl. Metastasis</i> 7(3):283-300 (1989)
C10	Bracke et al., "Tangeretin affects human mammary cell interactions," <i>Abstracts of Papers American Chemical Society</i> 219 (1-2): pAGFD 184 (2000)
C11	Breinholt et al., "Differential effects of dietary flavonoids on drug metabolizing and antioxidant enzymes in female rat," <i>Xenobiotica</i> 29(12):1227-1240 (1999)
C12	Carroll et al., "Anticancer properties of flavonoids, with emphasis on citrus flavonoids," <i>Flavonoids in Health and Disease</i> , Rice-Evans CA, Parker L, eds., Marcel Dekker Inc, NY, Chapter 19, pp. 437-446 (1998)
C13	Chaumontet et al., "Apigenin and tangeretin enhance gap junctional intercellular communication in rat liver epithelial cells," <i>Carcinogenesis</i> 15(10):2325-2330 (1994)
C14	Chaumontet et al., "Flavonoids (apigenin, tangeretin) counteract tumor promoter-induced inhibition of intercellular communication of rat liver epithelial cells," <i>Cancer Letters</i> 114:207-210 (1997)
C15	Chaumontet et al., "Lack of tumor-promoting effects of flavonoids: studies on rat liver preneoplastic foci and on <i>in vivo</i> and <i>in vitro</i> gap junctional intercellular communication," <i>Nutr. Cancer</i> 26:251-263 (1996)
C16	Chen et al., "Two new polymethoxylated flavones, a class of compounds with potential anticancer activity, isolated from cold pressed dancy tangerine peel oil solids," <i>J. Agric. Food Chem.</i> 45:364-368 (1997)
C17	Craig, "Foods that help fight cancer," <i>Vibrant Life</i> 14(4):16 (1998)
C18	Deschner et al., "Quercetin and rutin as inhibitors of azoxymethanol-induced colonic neoplasia," <i>Carcinogenesis</i> 12(7):1193-1196 (1991)
C19	Fang et al., "Studies on the chemical constituents from citrus reticulata," <i>Bulletin of Chinese Materia Medica</i> 10(2):29-30 (1985)
C20	Gilbert, "Vital signs: remedies; surprise finding on tamoxifen and citrus," <i>New York Times</i> F7 3/2/99 (1999)
C21	Guthrie and Carroll, "Inhibition of human breast cancer cell growth and metastasis in nude mice by citrus juices and their constituent flavonoids," <i>Biological Oxidants and Antioxidants: Molecular Mechanisms and Health Effects</i> , edited by Lester Packer and Augustine S.H. Ong, Aocs Press, Champaign, Illinois, Chapter 35 pp. 310-316 (1998)
C22	Guthrie and Carroll, "Inhibition of mammary cancer by citrus flavonoids," <i>Flavonoids in the Living System</i> edited by Mantey and Buslig, Plenum Press, New York, Chapter 16 227-236 (1998)
C23	Guthrie and Kurowska, "Anticancer and cholesterol-lowering activities of citrus flavonoids," <i>Handbook of Nutraceuticals and Functional Foods</i> , Edited by Robert E.C. Wildman, CRC Press, Chapter 7 pp. 113-126 (2001)
C24	Guthrie et al., "Combined effects of palm oil tocotrienols, flavonoids and tamoxifen on the proliferation of estrogen receptor-positive MCF-7 human breast cancer cells," <i>Proceedings of the American Association for Cancer Research</i> 37:280 (1996)
C25	Guthrie et al., "In vitro studies on anti-cancer and cholesterol-lowering activities of citrus flavonoids and limonoids," <i>FASEB Journal, Fed. of American Soc. For Experimental Biology, Bethesda, MD, US</i> 14(15):A563 (Mar. 2000)
C26	Hirano et al., "Citrus flavone tangeretin inhibits leukaemic HL-60 cell growth partially through induction of apoptosis with less cytotoxicity on normal lymphocytes," <i>British Journal of Cancer</i> 72:1380-1388 (1995)
C27	Hirano et al., "Natural flavonoids and lignans are potent cytostatic agents against human leukemic HL-60 cells," <i>Life Sciences</i> 55(13):1061-1069 (1994)



C28	Huachong, "Origin confirmation of a new natural product from <i>Oldenlandia diffusa</i> ," <i>Journal of Chinese Medicinal Materials</i> 21(6):301-302 (1998) [Chinese w/English abstract]
C29	Iwase et al., "Inhibitory effect of flavonoids from <i>Citrus</i> plants on Epstein-Barr virus activation and two-stage carcinogenesis of skin tumors," <i>Cancer Letters</i> 154:101-105 (2000)
C30	Kandaswami et al., "Antit proliferative effects of citrus flavonoids on a human squamous cell carcinoma in vitro," <i>Cancer Letters</i> 56:147-152 (1991)
C31	Kandaswami et al., "Differential inhibition of proliferation of human squamous cell carcinoma, gliosarcoma and embryonic fibroblast-like lung cells in culture by plant flavonoids," <i>Anti-Cancer Drugs</i> 3:525-530 (1992)
C32	Kawai, "Physiology of Fruits Juice: Cancer Retardant/Inhibitor in Citrus Juice" <i>Shokuhin Kogyo</i> pp35-43, June 2000
C33	Kawaii et al., "Antiproliferative activity of flavonoids on several cancer cell lines," <i>Biosci. Biotechnol. Biochem.</i> 63(5):896-899 (1999)
C34	Kawaii et al., "Effect of citrus flavonoids on HL-60 cell differentiation," <i>Anticancer Research</i> 19:1261-1269 (1999)
C35	Kawaii et al., "Quantitation of flavonoid constituents in <i>Citrus</i> fruits," <i>J. Agric. Food Chem.</i> 47:3565-3571(1999) [In Japanese, no English abstract available at time of filing]
C36	Kinoshita et al., "Differentiation induction of murine leukemia cells by flavonoids," <i>J. Pharmacobio-Dyn.</i> 8:s-122 (1985)
C37	Kinoshita et al., "Induction of differentiation in murine erythroleukemia cells by flavonoids," <i>Chem. Pharm. Bull.</i> 33(9):4109-4112 (1985)
C38	Lake et al., "Inhibition of xenobiotic-induced genotoxicity in cultured precision-cut human and rat liver slices," <i>Mutation Research</i> 440:91-100 (1999)
C39	Le Bon et al., "Inhibition of microsome-mediated binding of benzo[alpha]pyrene to DNA by flavonoids either <i>in vitro</i> or after dietary administration to rats," <i>Chem.-Biol. Interactions</i> 83:65-71 (1992)
C40	Malterud, "Flavonoids from <i>Orthosiphon spicatus</i> ," <i>Planta Medica</i> 55:569-570 (1989)
C41	Manthey et al., "Biological properties of citrus flavonoids pertaining to cancer and inflammation," <i>Current Medicinal Chemistry</i> 8:135-153 (2001)
C42	Manthey et al., "Methoxylated citrus flavones suppress cytokine expression by monocytes," Abstracts of Papers American Chemical Society 217(1-2):pMED1 212 (1999) [abstract]
C43	Manthey et al., "Polymethoxylated flavones derived from citrus suppress tumor necrosis factor-alpha expression by human monocytes," <i>J. Nat. Prod.</i> 62:441-444 (1999)
C44	Middleton and Kandaswami, "Potential health-promoting properties of citrus flavonoids," <i>Food Technology</i> pp. 115-119 (Nov. 1994)
C45	Murakami et al., "Inhibitory effect of citrus noiletin on phorbol ester-induced skin inflammation, oxidative stress, and tumor promotion in mice," <i>Cancer Research</i> 60:5059-5066 (2000)
C46	Murakami et al., "Suppressive effects of citrus fruits on free radical generation and nobiletin, an anti-inflammatory polymethoxyflavonoid," <i>BioFactors</i> 12:187-192 (2000)
C47	Rooprai et al., "Influence of putative antiinvasive agents on matrix metalloproteinase secretion by human neoplastic glia <i>in vitro</i> ," <i>Annals New York Academy of Sciences</i> 878:654-657 (1999)
C48	Rouseff and Nagy, "Health and nutritional benefits of citrus fruit components," <i>Food Technology</i> 125-126, 128-129,132 (Nov. 1994)
C49	Siess et al., "Mechanisms involved in the chemoprevention of flavonoids," <i>BioFactors</i> 12:193-199 (2000)
C50	So et al., "Inhibition of human breast cancer cell proliferation and delay of mammary tumorigenesis by flavonoids and citrus juices," <i>Nutrition and Cancer</i> 26(2):167-181 (1996)
C51	Soma et al., "Regulation of gene expression during redifferentiation of promyelocytic leukemia cells HL-60 by 12-O-tetradecanoylphorbol-13-acetate," <i>J. Pharmacobio-Dyn.</i> 8:s-123 (1985)
C52	Tsuchiya and Yamane, "Cotransport of Na <sup>+</sup> and amino acids in <i>Escherichia Coli</i> ," <i>J. Pharmacobio-Dyn.</i> 8:s-124 (1985)
C53	Vines, "Fruity formula could contain prostate cancer (Possible oral medication for containing prostate cancer)," <i>New Scientist</i> p. 18 (1995)

<b>EXAMINER</b>	<b>DATE CONSIDERED</b>
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	